REMARKS

I. Elections/Restrictions

The Examiner states on page 2 of the Office Action that restrictions to one of the following inventions is required under 35 U.S.C. § 121: (I) claims 1-8, drawn to a method of using an S-alkylthiol and (II) claims 9-11, drawn to an S-alkylthiol and a pharmaceutically acceptable carrier. Applicants hereby elect to prosecute the group I claims, claims 1-8.

The Examiner states on page 3 of the Office Action that Applicants are required under 35 U.S.C. § 121 to elect a single disclosed species for a specification on the merits to which the claim shall be restricted if no generic claim is finally held to be allowable. Applicants hereby elect to prosecute S-methylcysteine and S-methyl-L-cysteine as the elected species.

Applicants have cancelled claims 9-11 without prejudice. This cancellation does not necessitate changing the inventorship on the application.

II. Claim Rejection – 35 U.S.C. § 112

Claim 8 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which Applicants regard as the invention. The Examiner states that claim 8 is vague and indefinite since it recites "the dose ranges from 100mg." The range has no upper limit. The Examiner states that it would be clearer if Applicants amended the claim to read that the range is from 100mg to 10g as set forth on page 5 of the instant specification. Applicants have amended claim 8 accordingly by stating an upper limit as recited on page 5 of the specification to about 10g making the claim definite, thus alleviating this rejection.

III. Claim Rejections – 35 U.S.C. § 102

Claims 1, 2, 7, and 8 were rejected under 35 U.S.C. § 102(b) as being anticipated by Meisner. The Examiner states that even though the composition is administered to the patient for a different reason in the reference it would have been inherent to the process of Meisner that nitric oxide synthesis is inhibited since the steps of the processes (Meisner and the instant application) are the same. All the process requires is that the S-methylcysteine is administered to a patient. Applicants have amended claim 1 by using the transitional phrase "consisting essentially of" which has the effect of "limiting the scope to the specified component(s) and those which do not materially affect the basic and novel characteristics of the claimed invention." (See M.P.E.P § 2111.03) Applicants respectfully bring to the attention of the Examiner that the instant invention administers S-methylcysteine alone while the cited reference always administers S-methylcysteine in combination with three other components: biologically available calcium, ascorbic acid, tyrosine, and an anti-inflammatory substance selected from the group consisting of simple sugars, amino sugars, amino acids and derivatives thereof. The anti-inflammatory compounds include several amino sugars and amino acids with S-methylcysteine included as one of the alternative amino acids, but is not the "preferred" one (See Meisner col. 4, lines 55-60). As disclosed in the specification on page 2, nitric oxide synthesis inhibitors have not proven effective in the treatment of septic shock. S-methylcysteine and the other S-alkylthiols are not inhibitors of nitric oxide synthesis. It is Applicants belief that S-methylcysteine acts as an antagonist to S-nitrosocysteine and other S-nitrosothiols. Since nitric oxide produces some, but not all, of its effects by the formation of S-nitrosothiols, S-methylcysteine is also an antagonist to some of the effects of nitric oxide. It is Applicants belief that while the main action of S-methylcysteine is to inhibit binding of S-nitrosocysteine and

other nitrosothiols to putative binding sites, this may not be the only mechanism by which it works. As a result of S-alkylthiol being structural analogs of nitrosothiols, they partially counteract the actions of nitrosothiols and as a consequence also of nitric oxide.

Moreover, Meisner's patent is for a topical application or oral ingestion to aid wound healing that includes several active ingredients including various anti-inflammatory compounds. As stated previously, the anti-inflammatory compounds include several amino acids with S-methylcysteine included as one of the alternative amino acids. Certainly topical application will not produce any effects on blood pressure since polar compounds like S-methylcysteine are absorbed poorly through the skin, and whatever absorption might occur would be so slow that significant serum levels would not be achieved. While oral ingestion might result in higher blood levels, no hemodynamic effects have been shown. Therefore, it is unlikely that any oral administration as performed by Meisner of S-methylcysteine will produce any clinical effect.

Furthermore, while the effect of the other components on any actions of S-methylcysteine is unknown, it is certain that some of the other components have direct hemodynamic effects when administered intravenously which would obscure or confound any interpretation of the possible effects of S-methylcysteine. For example, absorbic acid prevents microvascular dysfunction in the skeletal muscle of the septic rat as shown by Armour et al. in the enclosed article from the Journal of Applied Physiology 90(3): 795-803 (2001). Similarly, tyrosine has been shown by Ekholm et al. to produce, particularly at high doses, marked bradycardiac and hypotensive responses.

Additionally, Applicants do not believe there is anticipation by Meisner because S-methyl-L-cysteine does not completely inhibit nitric oxide synthesis because it only selectively blocks the vasodilation caused by S-nitrosocysteine binding without affecting other nitric oxide

dependant vasodilations or other nitric oxide dependant processes (See page 7 of specification). Complete inhibition of nitric oxide synthesis blocks nitric oxide dependent vasodilation indiscriminately leading to ischemia and organ failure. Thus, S-methyl-L-cysteine is a discriminatory inhibitor, only blocking nitric oxide dependant processes. However, in the interest of expediting prosecution, Applicants have amended claim 1 to make it even clearer that the process of nitric oxide inhibition is not the same as those of Meisner, therefore it would not be inherent.

Applicants respectfully request the Examiner to reconsider claim 1 and to give meaning to the preamble because the Applicants believe the language of the preamble is necessary to give meaning to the claim and to properly define the invention. Diversitech Corp. v. Century Steps, Inc., 7 U.S.P.Q.2d 1315, 1317 (Fed. Cir. 1988). It is believed that the amendment to claim 1 should place claims 7 and 8, which depend from claim 1 in allowable form. Applicants respectfully request the Examiner to withdraw this rejection.

V. Claim Rejections – 35 U.S.C. § 103

Claims 3-6 were rejected under 35 U.S.C. § 102(b) as anticipated by or in the alternative, under 35 U.S.C. § 103(a) as obvious over Meisner. The Examiner states that even though the composition is administered to the patient for a different reason in the reference, it would have be inherent in the process of Meisner that the nitric oxide synthesis is inhibited since the steps of the processes (Meisner and the instant application) are the same. All the process requires according to the Examiner, is that the S-methylcysteine is administered to a patient. Applicants respectfully traverse this rejection.

"The general rule is that inherency may be relied upon where and only where the consequences of following the reference disclosure always inherently produces or results in the

claimed invention." See, e.g., W.L. Gore Associates Inc. v. Garlock Inc., 220 U.S.P.Q. 303, 314 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). As disclosed in the specification on page 2, nitric oxide synthesis inhibitors have not proven effective in the treatment of septic shock. S-methylcysteine and the other S-alkylthiols are not inhibitors of nitric oxide synthesis. It is Applicants belief that S-methylcysteine acts as an antagonist to S-nitrosocysteine and other S-nitrosothiols. Since nitric oxide produces some, but not all, of its effects by the formation of S-nitrosothiols, S-methylcysteine is also an antagonist to some of the effects of nitric oxide. It is Applicants belief that while the main action of S-methylcysteine is to inhibit binding of S-nitrosocysteine and other nitrosothiols to putative binding sites, this may not be the only mechanism by which it works. As a result of S-alkythiols being structural analogs of nitrosothiols, they partially counteract the actions of nitrosothiols and as a consequence also of nitric oxide.

Moreover, Meisner's patent is for a topical application or oral ingestion to aid wound healing that includes several active ingredients including various anti-inflammatory compounds. As stated previously, the anti-inflammatory compounds include several amino acids with S-methylcysteine included as one of the alternative amino acids. Certainly topical application will not produce any effects on blood pressure since polar compounds like S-methylcysteine are absorbed poorly through the skin, and whatever absorption might occur would be so slow that significant serum levels would not be achieved. While oral ingestion might result in higher blood levels, no hemodynamic effects have been shown. Therefore, it is unlikely that any oral administration as performed by Meisner of S-methylcysteine will produce any clinical effect.

The Examiner further states it is not clear from the reference if the S-methylcysteine is an S-methyl-L-cysteine form and it is not clear if the S-methylcysteine is a pharmaceutically

acceptable salt form. If the composition does contain S-methyl-L-cysteine or is not in a pharmaceutically acceptable salt form, then it would have been obvious to use either of these since L forms of amino acids are well known to exist in the body and pharmaceutically acceptable salt forms of amino acids are well known in the art since such salts are routinely used and pharmaceutical preparations to improve solubility, for example. not 102 rej

In order to prove a prima facie case of anticipation, one of the requirements is that the reference, under any of the subsections of Section 102, teach. That is, the reference must disclose the claimed invention, and must be available to the public. (See Irah H. Donner, Patent Prosecution: Practice & Procedure Before the U.S. Patent Office 321 (1998).) Because the prior art is required to teach and the Examiner states "it is not clear from the reference," it would appear that the prior art fails to teach, thus does not meet this requirement to make a prima facie case of obviousness. Applicants respectfully request Examiner to withdraw this rejection.

Applicants have submitted herewith the formal drawings, Figures 1-6, to the official draftsperson.

V. Conclusion

For the above-stated reasons, it is believed the Application is in a prima facia condition for allowance. Allowance is respectfully requested.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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AMENDMENT — VERSION WITH MARKINGS

TO SHOW CHANGES MADE

In the Specification

Please amend the specification as follows:

Page 5, line 16, delete "100" and insert--1--.

Page 7, line 15, delete "LPS" and insert--lipopolysaccharide--.

Page 8, line 16, delete "Figure" and insert--Figures--.

Page 8, line 16, after "1" insert-- -6--.

In the Claims

Please cancel claims 9-11.

Please amend the following claims:

1. (Amended)

A method of [inhibition of nitric oxide synthesis] counteracting the overproduction of nitric oxide which often occurs in hypotension an shock [comprising] consisting essentially of:

administering [a small but nitric oxide production inhibiting] to a patient a therapeutically effective amount of an S-alkylthiol [to a patient] as an antagonist of S-nitrosothiols.

7. (Amended)

The method of claim 1 wherein the administration is [by a method selected from the group consisting of oral, parenteral, enema, and topica] parenterally.

8. (Amended)

The method of claim 1 wherein the dose ranges from about [100] 1mg to about 10grams.